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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/409,122	03/22/95	JOYCE	J 19425

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EXAMINER	
SALIMI, A	
ART UNIT	PAPER NUMBER
1815	6

DATE MAILED: 04/03/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 12/27/96.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three month(s), or ~~thirty~~ days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-24 ~~is~~/are pending in the application.

Of the above, claim(s) 1-12 ~~is~~/are withdrawn from consideration.

☐ Claim(s) ______ is/are allowed.

☑ Claim(s) 13-24 ~~is~~/are rejected.

☐ Claim(s) ______ is/are objected to.

☐ Claims ______ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on ______ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on ______ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) ______.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: ______.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). ______

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

PTOL-326 (Rev. 10/95)

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1815.

Response to Amendment

This is a response to the amendment ***a***, paper No.5. Filed January 28, 1997. Claims 1-12 have been canceled. New Claims 13-24 are pending before the Examiner.

Claim Rejections - 35 USC § 112

Claims 17, 18, 23, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17 and 18 are vague and indefinite for not specifically reciting what is intended in "a pharmaceutical composition" beside the virus like particles. Is a pharmaceutical acceptable carrier intended?

Claim 23 is confusing in reciting "the L1 protein, the L1 protein".

Claim 24 is a duplicate of claim 13. Since SEQ ID NO:2 is the sequence encoded by SEQ ID NO:1, virus like particles comprised of the L1 protein having an amino acid sequence of SEQ ID NO:2 are identical to virus-like particles comprised of protein encoded by SEQ ID NO:1.

Claim Rejections - 35 USC § 112

Claims 15-20 are drawn to a vaccine, pharmaceutical composition, and a method of preventing papilloma virus infection using the recited vaccine. The specification does not teach or provide any guidance for development of a vaccine and method of prevention. There has been no showing that the nucleotide sequence of the current application provides a protection that is necessary for a vaccine , nor has there been any showing with regard to the prevention of papilloma virus infection utilizing the sequence of this application. Considering large quantity of experimentation needed, the unpredictability of the field, and the limited guidance in the specification, it is concluded that undue experimentation would be required to make and use the full scope of the intended claims.

Claim Rejections - 35 USC § 103

Claims 13-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowy et al (1992), Kirnbauer et al (1993), and Rose et al (1994). Lowy teaches a method of producing the recombinant HPV 16 capsid proteins in a host cell, whereby the host cell is a insect cell, yeast cell

or a mammalian cell. Lowy further teaches the procedures of purification of recombinant capsid proteins by CsCl or salt fractionation, the same method of instant application. Lowy further teaches that the recombinant capsid proteins of HPV can be used for vaccine development, and said vaccine can be used for preventing or treating against papilloma virus infection. Lowy does not use HPV18 as starting material to produce recombinant capsid proteins. Rose teaches a method of producing HPV18 recombinant capsid proteins in a yeast cell. Rose also suggests that VLPs can be used for vaccine development, both as therapeutically and prophylactic. Applicant in the amendment *a*, paper No.5. Filed January 28, 1997, page 8, argues that when applying 35 U.S.C. 103(a), one must closely review the claimed invention and the level of ordinary skill in the art in the pertinent art and then compare the claimed invention to the teachings of the prior art. Applicant further argues that the cited references fail to teach or suggest the instantly claimed invention, and contends that the benefit of obviousness was gained by teachings of the application. Applicant's arguments filed January 28, 1997 have been fully considered but they are not persuasive. First, the issue of level of ordinary skill when applied is intended to apply to a person at the Ph.D. level with the expertise in the field of molecular virology. Therefore, the skill level in this art is high. Second, the teaching of the prior art at the time of filing was compared to the application, Rose et al (1994) taught a method of expressing papilloma virus capsid protein L1 using baculovirus expression system including HPV-18, showed their binding capacity, and suggested their use as a vaccine. They further taught the production and purification of the virus particles in insect cell (claim 14, page 40). Lowy et al (1992) as stated in previous office action

taught a method of producing recombinant HPV-16 capsid protein in a host cell and isolation of protein using well known virology techniques employed to isolate virus particles. Thus, the prior art provides the teaching to obtain self assembled particles for HPV. Kirnbauer et al (1993) teach a method of isolating L1 of two human papilloma virus type 16 (HPV16) from condylomata acuminata, to investigate the possibility of alteration in L1 gene of the prototype HPV-16 (abstract). They further expressed the L1 capsid protein in insect cells using a baculovirus expression system, and showed high efficiency of self assembly of capsid proteins into a virus like particles, where they could be purified by density gradient (abstract). In addition, they doubly expressed L1 and L2 using baculovirus expression vector , and were also able to assemble virus particles in high yield. They further add that the employed method can be used as immunoprophylaxis and/or serological assay. Kirnbauer et al explain that the L1 gene obtained from the prototype HPV 16 DNA and used in previous studies might contain one or more mutations that inhibit self assembly due to lack of selective pressure for maintenance of an intact L1 gene. However, condylomata acuminata likely has maintained HPV genome that encode functional L1 proteins (page 6929, right column). They conclude that the efficient self assembly of HPV-16 particles may have implications to develop a vaccine against the said virus (bottom of the page 6935). This only differs from the claims in that they did not use HPV 18. Therefore, the prior art as evident by the cited references provide not only motivation i.e. serological assay; and vaccine, but also teach the necessary methods needed to succeed, and further add that isolation of L1 sequences from non-prototype samples contain several nucleotide mutation. Thus, the

observe mutation in the current sequence were expected over the prototype clones as taught in prior art. There has been no showing of unexpected results.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ali R. Salimi

3/25/97

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800